REMARKS

The Amendments

The Specification has been amended to identify the sequences on page 7, lines 4-5, as SEQ ID NO:5 and SEQ ID NO:6, respectively. Support is found in the sequence listing.

Claim 1 has been amended to spell out the abbreviations MC1R and MSH. Support is found on page 1, lines 18 and 22-23, of the Specification. Claim 1 has also been amended to incorporate the limitations of claims 11 and 15, which have been cancelled as redundant.

Claims 2-8 have been amended for better antecedent basis to specify that a further analog is administered. Support is found, e.g., at page 11, lines 1-5 of the Specification.

In addition, Claim 5 has been amended to identify the last two sequences as SEQ ID NO:5 and SEQ ID NO:6, respectively. Support is found on page 7, lines 4 and 5, of the Specification. Claim 5 has also been amended to include a "." at the end of the claim.

Claim 6 has been amended to include a "." at the end of the claim.

Claim 7 has been amended to recite "D-Lys^{11}" in the 21st compound and to separate the 24th-30th compounds with commas.

Non-elected claim 10 has been cancelled.

Claims 12 and 13 have been amended to correct a typographical error. Support is found, e.g., at page 16, lines 12 and 13 of the Specification.

No new matter has been added.

Claims 1-8 and 12-15 are pending. Claims 3, 4, 6 and 8 have been withdrawn from consideration.

Request for Rejoinder of Non-elected Claims

Rejoinder of non-elected claims 3, 4, 6 and 8 is respectfully requested. These claims have been made dependent or ultimately dependent on claim 1, and therefore with the allowance of claim 1, rejoinder is proper.

The Objections to the Claims

Claims 1, 5 and 7 have been objected to because of certain informalities: The Office Action states:

> Claim 1 refers to the abbreviations MC1R and MSH. These abbreviations should be spelled out the first time they are used in the claims (see the specification page 1).

Claim 1 has been amended to spell out the abbreviations MC1R and MSH.

The Office Action states:

> 37 CFR 1.821(d) states: "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." In the instant case, the last 2 sequences in claim 5 are SEQ ID NO:5 and SEQ ID NO:6 respectively. However, the words SEQ ID NO:5 and SEQ ID NO:6 do not appear in the claim.
>
> Claim 5 is objected to for not ending in a period. MPEP § 608.01 (m) states that, "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck,* 36 USPQ2d 1211 (D.D.C. 1995)."

Claim 5 has been amended to identify the last two sequences as SEQ ID NO:5 and SEQ ID NO:6, respectively. Claim 5 has also been amended to include a "." at the end of the claim.

The Office Action state:

> The 21st compound of claim 7 recites 'LYS'. Since all of the other amino acid abbreviations are of the form in which the first letter is capitalized and the other two letters are lower case, 'LYS' should appear as 'Lys'.
>
> Claim 7 uses commas to separate some of the compounds (see page 4), but other compounds (see the bottom of page 5) are not separated by commas. The claims should be of a consistent format.

Claim 7 has been amended to recite "D-Lys^{11}" in the 21st compound and to separate the 24th-30th compounds with commas.

Objections to the Specification

The Specification has been objected to for failing to use sequence identifiers for the sequences on page 7, lines 4-5. The Office Action states:

> 37 CFR 1.821(d) states: "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." In the instant case, the sequences of page 7 lines 4-5 are SEQ ID NO:5 and SEQ ID NO:6 respectively. However, the words SEQ ID NO:5 and SEQ ID NO:6 do not appear with the sequences.

The Specification has been amended to identify the sequences on page 7, lines 4-5, as SEQ ID NO:5 and SEQ ID NO:6, respectively.

The Rejections under 35 U.S.C. 112, second paragraph

Claims 1-2, 5, 7, 9 and 11-15 have been rejected under 35 USC 112, second paragraph as allegedly being indefinite. The Office Action states:

> Claim 1 and dependent claims 12-15 refer to an alpha-MSH analogue. It is noted that the specification (page 5 lines 19-25) defines the term analogue in terms of a derivative. However, the scope of 'derivatives' is unclear. There is not a standard art-recognized definition of derivative. As such, it is unclear what structural features, if any, are required by the derivatives. There is more than one reasonable interpretation of what falls within the scope of the claims. For example, it is unclear if any compound which contains a hydrogen (and meets the functional requirements) would be considered a derivative because the hydrogen

> is a shared element. It is noted that the applicants refer to examples of analogues. However, an exemplification is not the equivalent of an explicit, precise definition.

Claim 1 has been amended to specify a particular analogue. This clarifies the meaning of "analogue" as used in the claim. The remaining claims also specify particular analogues.

The Office Action also states:

> Claims 12 and 13 recite various variant alleles one of which is Asp194His (D294H). Since the variant refers to position 194 and 294 it is unclear if the variation occurs at the 194th position or at the 294th position or at both positions. As such, there is more than one reasonable interpretation of the claims.

Claims 12 and 13 have been amended to correct the typographical error in designating Asp294His.

The Office Action further states:

> Independent claims 1 and 11 refer to 'the steps of administering'. It is noted that the claims use the plural word 'steps' which implies more than one step. However, claims 1 and 11 only refer to one specific step - administration. It is unclear if the intent is that there are to be multiple administration steps or if the intent is that there is some other unnamed step. As such, it appears that the claims are incomplete or involve some type of error. It is noted that dependent claims 2, 5, 7, 9, 11-14 do not appear to recite any additional steps, while claim 15 appears to recite the step of identification.

Claim 1 has been amended to change "steps" to step.

The foregoing amendments should overcome the rejections.

The Rejections under 35 U.S.C. 112, first paragraph

Claims 1 and 12-15 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action states:

> [C]laims 1, 12-15 are drawn to methods of administering an analogue. Although unclear (see 112 2nd), the term analogue has been given the broadest

reasonable interpretation such that any structural similarity is sufficient to be classified as an analogue.

Claims 12-13 have been interpreted as being drawn to a variation at the 294th position (see page 2 line 8 of the specification). Claims 1,11 and dependent claims 2,5,7,9,11-14 have been interpreted as being drawn to a single step of administration.

(1) Level of skill and knowledge in the art/predictability in the art:
The level of skill in the art is high. There is unpredictability in predicting functional effects of replacements. It is not within the skill of the art to predict any and all replacements that would result in derivatives in which the resulting compound exhibits agonist activity for the melanocortin-1 receptor.

(2) Scope of the invention/Partial structure/disclosure of drawings:
In the instant case, the claims 1,12-15 are drawn to methods of administering an analogue. Although unclear (see 112 2nd), the term analogue has been given the broadest reasonable interpretation such that any structural similarity is sufficient to be classified as an analogue. Claims 12-13 have been interpreted as being drawn to a variation at the 294th position (see page 2 line 8 of the specification). Claims 1, 11 and dependent claims 2, 5, 7, 9, 11-14 have been interpreted as being drawn to a single step of administration. In considering the size of the genus, if six of the 13 amino acids of MSH were replaced with any of the 20 naturally occurring amino acids (i.e. derivatives) there are at least 20^6(i.e. 64000000) different compounds. Further, there are many non-natural amino acids and other chemical compounds that could be considered derivatives. As such, the genus is large.

The specification, for example claims 5 and 7 (which are not included in this rejection) provides examples of analogues. However, the compounds represent a small fraction of the possible variety of compounds in the genus. One of skill in the art would not recognize that applicant was in possession of the claimed genus. There is substantial variability in the genus. Since there are a substantial variety of compounds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) *Functional characteristics:*
The analogues are defined to exhibit agonist activity for the melanocortin-1 receptor. However, there is no specific disclosed correlation between structure and function. It is unclear what structural elements are required for the recited function. There are no common attributes or characteristics that identify the agonists. As such, one of skill in the art would not recognize a core structure, common attributes, or features of the agonists. One of skill in the art would not recognize agonists outside of those specifically identified. There is no teaching in

the specification regarding what part of the structure can be varied while retaining the ability to be an agonist. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention/actual reduction to practice:
The specification, for example claims 5 and 7 (which are not included in this rejection) provides examples of analogues and refers to other analogues (page 2 last paragraph).However, such compounds are not representative of the instant genus nor do the compounds provide a specific correlation between structure and function such that one could identify any and all agonists.

As stated *supra,* the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,12-15 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder,* 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

With this amendment the claims specify particular analogues, which should obviate the rejection.

The Rejections under 35 U.S.C. 103(a)

Claims 1-2, 5, 7, 9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al (JAMA 1991 266(19):2730-2736 as cited in IDS 8/29/06) and Epitan (Epitan 2001 Annual Report 36 pages, accessed from http://www.clinuvel.com.au/resources/pdf/annual_reports/Annual_Report_2001.pdf) and Bastiaens et al (Am J Hum Genet 2001 68(4):884-894 as cited in IDS). The Office Action states:

> Levine teach the administration of [Nle4,D-Phe7]-alpha-MSH to men with skin type I or II, for example, to induce skin tanning (page 2730). Levine recognize a need to treat those at risk for skin cancer who burn easily and state that a strategy is to produce tanning without sun exposure (page 2730 last paragraph). Levine teach that the [Nle4,D-Phe7]-alpha-MSH peptide has desirable properties including improved potency and stability over alpha-MSH (page 2731 column 1, page 2735 3rd column). Levine conclude (page 2734 3rd column) that those humans who were administered [Nle4,D-Phe7]-alpha-MSH had increased skin pigmentation and that subjects who tan poorly responded to the treatment.
>
> Levine does not expressly teach administration to subjects who have an MC1R variant allele.
>
> Levine recognize a need to treat those at risk for skin cancer who burn easily and state that a strategy is to produce tanning without sun exposure (page 2730 last paragraph). Levine teach the use of [Nle4,D-Phe7]-alpha-MSH (page 2730).
>
> Epitan also recognize a need to treat those at risk for skin cancer and discuss the use of Melanotan (also known as [Nle4,D-Phe7]-alpha-MSH) (actual page 3, listed as page number 01; page 4). Epitan refers to the Levine article (page 4 3rd column) and stated that the results demonstrate that the drug could be used to induce a natural tan in human beings. On page 13 (listed as page 10 11) Epitan teach that studies have shown that an increased skin cancer risk is attributed to individuals with abnormal melanocyte receptors in the skin and studies will determine the individuals whom would most benefit from treatment. Thus one would be motivated to treat specific patients who would benefit from the treatment. Epitan does not expressly list specific abnormal melanocyte receptors.
>
> Bastiaens teach that MC1R gene variants are important independent risk factors for skin cancer (abstract, page 891 2nd column). Bastiaens teach that carriers with two variant alleles were at an increased risk for developing cell carcinoma (abstract, page 892 first column) and Bastiaens mention Asp84Glu, and Asp294His as alleles having the highest relative risks (abstract, see also Table 2 and 4). Bastiaens also recognize that fair skin and red hair are associated with an increased risk of melanoma (page 884). Bastiaens recognize that alpha-MSH has effects on melanocytes (page 885). Bastiaens report a patient population with

various skin types including type I and II (Table 1). It is noted that Bastiaens report detecting MC1R gene variants (page 887 2nd column) but does not report the use of the primers as in claim 15 of the instant invention.

Since Levine and Epitan motivate the use of [Nle4,D-Phe7]-alpha-MSH for specific patient populations and Epitan specifically teach human individuals with abnormal melanocyte receptors one would be motivated to administer [Nle4,D-Phe7]-alpha-MSH to humans with abnormal melanocyte receptors. Since Bastiaens teach that MC1R (melanocortin-I receptor) gene variants are important independent risk factors for skin cancer (abstract, page 891 2nd column) and specifically point to Asp84Glu, and Asp294His as alleles having the highest relative risks (abstract, see also Table 2 and 4) one would be motivated to administer [Nle4,D-Phe7]- alpha-MSH to humans with the Asp84Glu, and Asp294His alleles. One would have a reasonable expectation of success since Levine conclude (page 2734 3rd column) that those humans who were administered [Nle4,D-Phe7]-alpha-MSH had increased skin pigmentation and that subjects who tan poorly responded to the treatment.

Since the references obviate the administration of [Nle4,D-Phe7]-alpha-MSH the compound limitations of claims 1-2, 5, 7, 9, 11 are met. Since the references obviate the administration to those with MC1R variant alleles especially Asp84Glu, and Asp294His as well as those with for skin including types I and II the patient population of claims 1, 11-14 are met.

Since the references motivate the use of [Nle4,D-Phe7]-alpha-MSH to induce skin pigmentation one would be motivated to administer an effective amount as recited in the instant claims.

In the instant case, the references recognize a need to treat those at risk for skin cancer who burn easily, for example. Levine and Epitan set forth the use of a particular compound to achieve such goal. Epitan motivates the administration to a specific sub-population of patients (those with abnormal melanocyte receptors) and Bastiaens teach facts about abnormal melanocyte receptors and the related cancer risk. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Although unclear (see 112 2nd), the term analogue has been given the broadest reasonable interpretation such that any structural similarity is sufficient to be classified as an analogue. Claims 12-13 have been interpreted as being drawn to a variation at the 294th position (see page 2 line 8 of the specification). Claims 1, 11 and dependent claims 2, 5, 7, 9, 11-14 have been interpreted as being drawn to a single step of administration.

It is noted that claim 15 was not included in this rejection. With this amendment, all claims specify the limitations of claim 15. Both the EPITAN 2001 report and the Levine reference are silent on the primers of claim 15. Also Bastiaens is silent on the primers of claim 15 (see Bastiaens page 887, right hand column, bottom paragraph and page 888, left hand column top paragraph). Thus, it is believed the amendments have overcome this rejection.

Conclusion

This application appearing to be in condition for allowance, passage to issuance is respectfully requested. It is believed a three-month extension of time is due with this response, and is submitted herewith through the Electronic Filing System. Please deduct the correct fee from deposit account 07-1969.

Respectfully submitted,

/ellenwinner/

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November 23, 2009